EXHIBIT 14

News
Press kits
Media contacts

Acambis awarded second US Government MVA smallpox vaccine contract

Cambridge, UK and Cambridge, Massachusetts – 30 September 2004 – Acambis plc ("Acambis") (LSE: ACM, NASDAQ: ACAM) announces that its subsidiary, Acambis Inc., has been awarded a contract potentially worth up to $131m by the National Institute of Allergy and Infectious Disease ("NIAID"), part of the US National Institutes of Health, for the manufacture and development of a Modified Vaccinia Ankara ("MVA") vaccine. Acambis is co-developing its MVA vaccine candidate with Baxter Healthcare SA ("Baxter").

MVA is a weakened form of smallpox vaccine that is being developed for use in people for whom the traditional smallpox vaccine is contraindicated, such as patients with disorders of the immune system or skin conditions such as eczema.

The NIAID funding is split between core contract requirements and an optional manufacturing section. The core component of the contract, worth approximately $76m, requires Acambis to manufacture, fill, finish and release 500,000 single-dose vials of MVA and to carry out development work. The clinical testing programme, which is expected to continue into 2007, includes: safety and immunogenicity studies in healthy adults and target-population subjects; a dose-response study; and trials involving both vaccinia-naïve and previously vaccinated subjects.

The optional element of the contract, worth an additional $55m, would require manufacture, fill, finish and release of up to a further 2.5 million single-dose vials of MVA.

This is the second contract the Acambis-Baxter partnership has been awarded by the US Government for MVA. It received an initial $9.2m contract in February 2003 for development of its MVA vaccine candidate, manufacture of several thousand doses and clinical testing in a Phase I trial, which is ongoing. Incorporated into the new, second contract is work that was originally proposed to take place under an optional "Part B' of the first contract, including clinical testing in healthy adults and at risk subjects.

In its second Request for Proposals, the NIAID indicated it was targeting MVA vaccine candidates that can be produced at commercial scale and have demonstrated safety and immunogenicity in extensive pre-clinical studies.

The US Government has indicated its intention to procure a stockpile of an attenuated smallpox vaccine, such as MVA, as part of its defence against the threat of smallpox virus being used as a bioterrorist weapon, for which Acambis and Baxter plan to tender in due course.

Acambis' MVA vaccine was recently granted fast-track designation by the US Food and Drug Administration.

Gordon Cameron, Chief Executive Officer, said:

"Being awarded this contract means that we continue to be well positioned to compete for US Government supply contracts for an MVA stockpile. We are confident that the Acambis-Baxter partnership represents a very strong proposition, combining our expertise in government contracting and product development with Baxter's considerable manufacturing track record.'

-ends-

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About Acambis:
Acambis is a leading developer of vaccines to prevent and treat infectious diseases. Recognised internationally as the leading producer of smallpox vaccines, Acambis is developing an investigational second-generation smallpox vaccine and manufacturing emergency-use stockpiles of this investigational vaccine for the US Government and other governments around the world. Acambis is establishing a travel vaccines franchise through its US-based subsidiary Berna Products Corporation, which markets Vivotif®, the world's only licensed oral typhoid vaccine, in North America. Acambis has a number of other potential travel vaccines in development and is also developing an investigational vaccine against the West Nile virus, which has spread to 46 US States in the last five years.

Acambis is based in Cambridge, UK and Cambridge, Massachusetts, US. Its primary listing is on the London Stock Exchange (ACM) and its shares are listed in the form of American Depositary Receipts on NASDAQ (ACAM). More information is available at www.acambis.com.

"Safe Harbor' statement under the Private Securities Litigation Reform Act of 1995:
The statements in this news release that are not historical facts are forward-looking statements that involve risks and uncertainties, including the timing and results of clinical trials, product development, manufacturing and commercialisation risks, the risks of satisfying the regulatory approval process in a timely manner, the need for and the availability of additional capital. For a discussion of these and other risks and uncertainties see "Risk factors' in the Company's 2003 Annual Report and 2003 Form 20-F, in addition to those detailed in the Company's filings made with the Securities and Exchange Commission from time to time. These forward-looking statements are based on estimates and assumptions made by the management of Acambis and are believed to be reasonable, though are inherently uncertain and difficult to predict. Actual results or experience could differ materially from the forward-looking statements.

Contract Awards -- FY 2004

To sort this table, click the header in each column. To sort in the opposite direction, click again.

Dollars shown are for the full term of the contract

ID No. SORT	RFP SORT	TITLE SORT	CONTRACT SORT	CONTRACTOR SORT	AMOUNT SORT
04-01	DIR-04-01	Operation of a Facility for the Testing of Malaria Vaccines in Adult Human Subjects	HHSN266200400077C, N01-AI-40077	Johns Hopkins University	$13,738,436
04-01	DMID-PR2004-01	Neutralizing Monoclonal Antibodies for Type A Botulinum Neurotoxins	HHSN266200500004C, N01-AI-50004	XOMA (US) LLC	$15,000,000
04-07	DAIT-04-07	Atopic Dermatitis and Vaccinia Network: Animal Studies Consortium	HHSN266200400030C	Children's Hospital Corporation	$10,031,776
04-08	DAIT-04-08	Atopic Dermatitis and Vaccinia Immunization Network (ADVN): Statistical and Data Coordinating Center (SDCC)	HHSN266200400033C	Rho Federal Systems Division, Inc.	$10,089,624
04-09	DMID-04-09	Sexually Transmitted Infections Clinical Trials Group	HHSN266200400074C, N01-AI-40074	The Regents of the University of California, San Francisco	$20,593,306
04-09	DMID-04-09	Sexually Transmitted Infections Clinical Trials Group	HHSN266200400073C, N01-AI-40073	University of Alabama at Birmingham	$5,875,168
04-10	DMID-04-10	Malaria Vaccines: Clinical research and Trial Sites in Endemic Areas	HHSN266200400014C	Noguchi Memorial Institute for Medical Research	$8,743,860
04-17	DMID-04-17	Development, Testing and Evaluation of Candidate Vaccines Against Plague	HHSN266200400034C, N01-AI-40034	Avecia Limited	$27,664,200
04-18	DAIT-BAA-04-18	Population Genetics Analysis Program: Immunity to Vaccines/Infections	HHSN266200400065C, N01-AI-40065	Mayo Clinic Rochester	$10,258,094
04-18	DAIT-BAA-04-18	Population Genetics	HHSN266200400067C,	Research	$26,419,308

		Analysis Program: Immunity to Vaccines/Infections	N01-AI-40067	Triangle Institute	
04-18	DAIT-BAA-04-18	Population Genetics Analysis Program: Immunity to Vaccines/Infections	HHSN266200400064C, N01-AI-40064	DecCode Genetics	$23,879,659
04-18	DAIT-BAA-04-18	Population Genetics Analysis Program: Immunity to Vaccines/Infections	HHSN266200400069C, N01-AI-40069	University of Washington	$7,778,427
04-18	DAIT-BAA-04-18	Population Genetics Analysis Program: Immunity to Vaccines/Infections	HHSN266200400068C, N01-AI-40068	The Board of Trustees of the University of Alabama for The University of Alabama at Birmingham	$11,797,640
04-18	DAIT-BAA-04-18	Population Genetics Analysis Program: Immunity to Vaccines/Infections	HHSN266200400066C, N01-AI-40066	McMaster University	$14,827,281
04-21	DMID-04-21	TB Vaccine Testing and Research Materials	HHSN266200400091C, N01-AI-40091	Colorado State University	$25,167,768
04-22	DMID-04-22	Assessing Safety of Cell Substrates and Vaccine Components, Part E: Develop, characterize and validate assays for detection of novel or latent/occult adventitious agents in cell substrates	HHSN266200400100C	ISIS Pharmaceuticals	$5,613,317
04-23	DAIDS-04-23	Master Contract for Preclinical Development	HHSN2662004000045C	Advanced BioScience Laborties, Inc.	$31,019,359
04-24	DAIT-04-24	Development of Immune Monitoring Reagents and MHC Typing Technologies for Non-Human Primates (Part II)	HHSN266200400088C	University of Wisconsin-Madison	$6,487,545
04-24	DAIT-04-24	Development of Immune Monitoring Reagents and MHC Typing Technologies for Non-Human Primates (Part I)	HHSN26620040101C	Beth Israel Deaconess Medical Center	$5,867,622
04-24	DAIT-04-24	Development of Immune Monitoring Reagents and MHC Typing Technologies	HHSN266200400087C	University of New Mexico	$6,984,988

		for Non-Human Primates (Part II)			
04-30	DAIDS-04-30	Patient Safety Monitoring in International Laboratories	HHSN266200500001C, N01-AI-50001	Johns Hopkins University	$15,840,002, Option: $28,652,62
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400042C	The University of Chicago	$18,113,696
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400041C, N01-AI-40041	Northrup Grumman IT Federal Enterprise Solutions	$16,960,155
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400040C, N01-AI-40040	Systems Research and Applications Corporation	$13,648,416
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400039C, N01-AI-40039	University of Notre Dame	$9,986,810
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400038C, N01-AI-40038	The Institute for Genomic Research	$21,110,385
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400037C	Trustees of the University of Pennsylvania	$9,348,340
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400036C, N01-AI-40036	Board of Trustees for the University of Alabama at Birmingham	$6,868,934
04-34	DMID-04-34	Bioinformatics Resource Centers for Biodefense and Emerging/Re-emerging Infectious Diseases	HHSN266200400035C, N01-AI-40035	Virginia Polytechnic Institute and State University	$10,361,305
04-38	DAIT-BAA-04-38	Innate Immune	HHSN266200400044C,	Coley	$16,902,114

		Receptors and Adjuvant Discovery	N01-AI-40044	Pharmaceutical Group	
04-38	DAIT-BAA-04-38	Innate Immune Receptors and Adjuvant Discovery	HHSN266200400043C, N01-AI-40043	VaxInnate Corporation	$4,863,086
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400079C, N01-AI-40079	Vanderbilt University Medical Center	$4,743,637
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400080C, N01-AI-40080	Torrey Pines Institute for Molecular Studies	$4,801,804
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400081C, N01-AI-40081	Oregon Health & Science University	$4,635,812
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400082C, N01-AI-40082	Duke University Medical Center	$6,976,293
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400083C, N01-AI-40083	Center for Biological Sequence Analysis (CBS) BioCentrum, Technical University of Denmark	$3,751,185
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400084C, N01-AI-40084	Imperial College, Department of Infectious Diseases	$4,480,000
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400085C, N01-AI-40085	Johns Hopkins School of Medicine	$7,279,857
04-39	DAIT-04-39	Large-Scale Antibody and T Cell Epitope Discovery Program	HHSN266200400086C, N01-AI-40086	The University of North Carolina at Chapel Hill, Office of Sponsored Research	$3,552,062
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN2662005000016I, N01-AI-50016	Board of Trustees of the University of Illinois	$150,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400098I	Cellular Technology Limited	$80,000,000

04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400097I	University of Texas Medical Branch	$80,000,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400096I	IIT Research Institute	$80,000,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400095I	Lovelace Respiratory Research Institute	$80,000,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400094I	Battelle Memorial Institute	$80,000,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400092I	Health Protection Agency	$80,000,000
04-40	DMID-04-40	In Vitro & Animal Models for Emerging Diseases and BioDefense	HHSN266200400093I	The Board of Trustees of the University of Illinois College of Medicine, Department of Pharmacology Toxicology Research Laboratory	$80,000,000
04-44	DAIT-04-44	Regulatory Management Center	HHSN266200400089C	Social & Scientific Systems	$6,028,783
04-46	DAIT-04-46	Immune Tolerance Network-Clinical Site Monitoring Group	HHSN266200400070C, N01-AI-40070	PPD Development, LP	$12,263,968
04-48	DMID-04-48	Development, Testing and Evaluation of a Live Attenuated (LVS) Vaccine Candidate	N01-AI-40002	DynPort Vaccine Company, LLC	$570,527
04-49	DMID-04-49	Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine	HHSN266200400071C, N01-AI-40071	Acambis, Inc.	$76,283,309
04-49	DMID-04-49	Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine	HHSN266200400072C, N01-AI-40072	Bavarian Nordic	$100,570,172
04-59	DAIT-04-59	Data Coordinating Center for the	HHSN266200400075C, N01-AI-40075	PPD Development, LP	$13,095,790

		Immune Tolerance Network (ITN)			
04-61	DMID-04-61	Development and Production of an Investigational Inactivated H5 (2004) Influenza Vaccine for Use in Phase I/II Clinical Trails	HHSN266200400031C	Aventis Pasteur Incorporated	$2,362,639 Option: $2,146,168
04-62	DMID-04-62	Development and Production of an Inactivated (2004) H5 Influenza Vaccine for Use in Phase I/II Clinical Trials	HHSN266200400032C, N01-AI-40032	Chiron Corporation	$2,040,362 Option: $763,740
04-67	DMID-04-67	Travel and Conference Support Services	HHSN266200400104C, N01-AI-40104	KRA Corporation	$1,500,000

See Contract Awards from other years.

Return to the main R&D Contracts Web page.

EXHIBIT 15

OMB No. 0990-0115

Electronic Request for Proposal
SECTION A – SOLICITATION/CONTRACT FORM

OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE http://www.niaid.nih.gov/contract/default.htm FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.

Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.

RFP Number:	Just In Time:	Small Bus. Set-Aside	[ ]Yes [X]No	Level of Effort:
		8(a) Set-Aside	[ ]Yes [X]No	[ ] Yes [X] No
NIH-NIAID-DMID-03-44	[ ] Yes	NAICS Code	541710	Total Effort:
	[X] No	Size Standard	500 employees	[N/A]

TITLE:
Development and Testing of a Modified Vaccinia Ankara (MVA) Vaccine

Issue Date: August 15, 2002	Due Date: September 30, 2002 Time: 4:00 PM, EST	Technical Proposal Page Limits: [ ] Yes *(see "How to Prepare and Submit Electronic Proposals")* [X] No

ISSUED BY:

Jacqueline C. Holden
Contracting Officer
Contract Management Branch, DEA
NIH, NIAID
6700-B Rockledge Drive
Room 2230, MSC 7612
Bethesda, MD 20892-7612

[ ] ***We reserve the right to make awards without discussion.***

NO. OF AWARDS:

[ ] Only 1 Award
[X] Multiple Awards

PERIOD OF PERFORMANCE:

Part A: 3 years beginning on or about 01/31/2003
Part B, Option: Up to 24 Months

Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See SECTION J - Attachments)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. The paper copy with original signatures is the official copy for recording timely receipt. If the paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

POINT OF CONTACT **– Phil Hastings** ***--COLLECT CALLS WILL NOT BE ACCEPTED--***

Telephone: Direct **301-496-0194** *Main* **301-496-0612**	*Fax* **301-402-0972**	*E-Mail* ph23k@nih.gov

Updated thru FAC 2001-07 (05/15/02)

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PLEASE NOTE: If you intend to submit a proposal in response to this RFP, you are requested to submit a **PROPOSAL INTENT RESPONSE SHEET** by **Monday, September 9, 2002.** Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

BACKGROUND / STATEMENT OF WORK / NOTES TO OFFERORS
Background

Development and Testing of a Modified Vaccinia Ankara (MVA) Vaccine
RFP NIH-NIAID-DMID-03-44

The National Institute of Allergy and Infectious Diseases (NIAID) is the primary institute at the National Institutes of Health (NIH) for emerging infectious disease research, including research on pathogens that can be used as agents of bioterrorism. Bioterrorism is defined as the use of microorganisms that cause human disease, or the toxins released from them, to harm people or elicit widespread fear or intimidation of society.

The events of the past year have significantly changed the world's perception of the nature and degree of the threats posed by the use of infectious agents as weapons of bioterrorism. The risk of using such weapons once appeared to be restricted to military encounters. However, the deliberate exposure of postal workers, other government employees and the American public at large to *Bacillus anthracis* spores highlighted the need to devise appropriate and effective measures to protect all U.S. citizens from the harmful effects of those biologic agents of most concern.

Smallpox is an infectious disease caused by the variola virus, a member of the orthopox family. The global eradication of smallpox in 1980 has been heralded as one of the most significant feats of mankind. In 1971, the last case of smallpox in the Americas was seen. Shortly thereafter, routine smallpox immunization was discontinued in the U.S. because the risk of vaccination outweighed the threat of the disease. Recent knowledge on the weaponization and availability of smallpox stocks to rogue nations has increased concern about the population's vulnerability to this disease. As a result of this assessment, the U.S. government is currently procuring enough smallpox vaccine for every U.S. citizen.

The vaccine that contributed to the eradication of smallpox was based on a live, replicating vaccinia virus that had been attenuated over time through serial passages in tissue culture. This vaccine is reactogenic, causing common side effects such as redness and swelling at the site of vaccination, fever, or muscle aches in over 90% of people. Although rare in healthy recipients of the vaccine, vaccination with vaccinia can cause encephalitis, eczema vaccinatum, disseminated vaccinia and even death. The frequency of these events is increased as the ability to control the vaccinia replication is decreased such as when a person's immune system becomes increasingly compromised. The number of U.S. citizens at risk for these rare events has increased over the years due to life-saving drugs and medical procedures which compromise the immune system such as those drugs administered following organ transplant and the increased number of cases of HIV-infection. This fact has raised concerns about the wisdom of vaccinating every U.S. citizen with live, replicating vaccinia vaccine, should that need arise.

Modified Vaccinia Ankara (MVA) is a strain of vaccinia that has been further attenuated by serial passage in chick embryo fibroblasts. MVA has a substantial clinical history due to its extensive use as a vaccine to immunize over 120,000 people during the smallpox mass vaccination campaign in Germany in the 1970 s. In most human and primate cells, replication of the virus is blocked at the final stages of maturation, but most of the viral proteins are produced. Very limited replication (less than two plaque forming unit/cell) is seen in some mammalian cell lines. The gene deletions (approximately 33kbp) associated with MVA have been partially characterized. At least two host range genes are absent, as are the genes associated with at least four immunomodulatory proteins. Both neutralizing and hemagglutination inhibition antibodies are, however, produced. There is also some evidence that MVA can protect against variola virus challenge in monkeys. Most recently tested as an experimental vaccine vector for the delivery of other vaccine candidates, including HIV and cancer vaccines, the safety profile has been expanded to include contemporary data in recipients with potential immunocompromised status.

To address the urgent and compelling need to accelerate the development and stockpiling of MVA smallpox vaccines, the government has developed a comprehensive approach that includes both collaborative opportunities with NIAID as well as contract awards. Collaborative opportunities are <u>not</u> the subject of this Request for Proposals (RFP), however it is briefly described here for the sake of completeness. Collaborative opportunities from NIAID are available to all legitimate parties and include: the availability of a master seed stock of MVA from NIAID; the availability of some characterized reagents and standard operating procedures (SOPs) for immunologic measurements; assistance in evaluating Investigational New Drug (IND) grade vaccine candidates in relevant animal models; and assistance with testing of IND vaccine candidates in clinical trials through the NIAID clinical trials contract network. Further information regarding the requirements for requesting collaborative opportunities is described below.

It is the intent of the Government to provide contract support for the development and stockpiling of MVA vaccines through the issuance of three sequential Request for Proposals (RFPs). The first procurement action and the subject of this RFP (NIAID-DMID-03-44) is intended to provide resources for the initial development of MVA vaccine candidates. In addition, the Government intends to issue a second RFP during the summer of 2003, entitled "Production and Acquisition of MVA Vaccine." The objective of the second RFP will be to manufacture, formulate, fill and finish, and test, in accordance with cGMP regulations, up to 30 million doses of MVA vaccine to constitute the U.S. Government's stockpile for emergency use under IND, and to provide a licensure plan to include the conduct of expanded human safety studies required for licensure and the conduct of pivotal animal protection studies. A third contract action for the acquisition of a licensed product is being planned for 2005, under the auspices of the Centers for Disease Control (CDC).

Participation in NIAID's initial RFP (NIAID-DMID 03-44) will not be a pre-requisite for participation in subsequent MVA vaccine procurements planned by the NIAID and the CDC.

Information Required to Request
Consideration for NIAID Collaborative Opportunities

1. Evidence that the offeror/requestor/interested party has secured access to all intellectual property, know-how and tangible materials for this proposed work, or has a plan to secure such intellectual property, know-how and tangible materials.

2. Characterization data for the vaccine candidate that demonstrates manufacturing, control and safety features. Data should include, but not be limited to, the following:

    a. Chemistry, manufacturing and control testing information to include:

        i. Documentation of all raw materials used in the production of the master and working seed viruses and any cell substrates used in the production of the vaccine. All animal derived materials used in the production of the master seeds or cell banks as well as the manufacturing of the vaccine should be described and the country of origin of the animals should also be provided. Tabular form is requested.

        ii. Description of the production of the seed virus and cell banks used in vaccine production. Inclusion of a flow diagram is requested.

3. Description of vaccine production. Inclusion of a flow diagram is requested.

4. Summary of all process and release testing and the respective data to assess purity, potency, and safety of the product.

5. Data to support the stability and consistency of manufacturing. Examples of the type of stability for MVA includes demonstration of the stability of the genotype and phenotype and inclusion of a complete evaluation of the non-replicative/or limited replication of the vaccine candidate in multiple mammalian cell lines.

6. Pre-clinical safety data to include:

    a. Data demonstrating the safety of the candidate vaccine as well as the design of the preclinical studies used in the assessment.

    b. Data to support the lack of/or limited replication in animals and the stability of the genetic phenotype.

7. Documentation that the vaccine candidate can elicit an immune response in animals. Rationale for the choice of the animal model used and the regimen evaluated should also be included.

8. All animal data evaluating vaccine dosage and immunization regimens.

9. Any additional pre-clinical data to demonstrate "proof of concept", effectiveness. Protocols should also be included.

For more information regarding collaborative opportunities with NIAID, please contact Deborah Katz of the Office of Biodefense Research Affairs, DMID/NIAID, at dkatz@niaid.nih.gov.

Statement of Work – PART A
Development and Testing of a Modified Vaccinia Ankara (MVA) Vaccine
RFP NIH-NIAID-DMID-03-44

Introduction

This RFP (NIH-NIAID-DMID-03-44), for the initial development of MVA vaccine candidates, consists of 2 parts. Part A addresses development, manufacturing, testing and the conduct of Phase I studies in healthy populations. Specifically, the main objectives of Part A are to:

- Develop an MVA vaccine. This will include the development of the product as well as preparation of the chemistry, manufacturing and control (CMC) data to support use of this product under an IND application submitted to the Food and Drug Administration (FDA).
- Assess protection and immunogenicity provided by MVA vaccines in appropriate animal models.
- Conduct Phase I clinical trials to assess the safety and immunogenicity of MVA candidate vaccines.
- Develop a feasibility plan to manufacture and fill at least 30 million doses of MVA vaccine under current Good Manufacturing Processes (cGMP). This plan will include product characterization and product release and stability testing. The plan will also include production and testing of diluents, preservatives and other final ingredients that may be required.

Part B is an option to this contract requirement and, if exercised by the Government, will provide for the conduct of expanded Phase II clinical studies in healthy populations (i.e., adults and children) and Phase I and II studies in "at risk" (i.e., immunocompromised) populations.

Offerors must submit proposals for both Part A and Part B. For Part A, multiple awards may be made. For the Part B option, if exercised, the Government will select the candidate vaccine(s) that meet the milestones outlined in the Statement of Work and show the best potential of being a successful MVA vaccine candidate. Contract(s) awarded under this RFP will be milestone and product driven. Therefore, following each milestone and the subsequent review by NIAID staff, down-selection (i.e., discontinuation of contract support by means of early contract termination) may occur based on the quality of products, results of pre-clinical testing, or if Statement of Work milestones are not met.

The U.S. Government has determined that the urgent nature of the current threat requires an accelerated pace of development, testing, approval and procurement of an emergency stockpile of this vaccine. Although future smallpox vaccines may be derived from other strains, formulated in a different manner, or based on another platform these novel approaches are not being considered for this solicitation due to the urgent need.

Statement of Work – Part A

Independently, and not as an agent of the government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government as needed to perform the work described below.

This procurement will be milestone-driven and awarded in phases. Periodic assessments of progress and continuation of subsequent milestones will be based on timeliness and quality of deliverables and consultations between the contractor and NIAID program staff. **Cost proposals must be prepared based on the estimated cost of each milestone.**

A. Using technology known to be acceptable in the production of vaccines licensed for use in the U.S., develop a prototype MVA vaccine that will protect against challenge in relevant animal models.

1. Milestone 1: Within three months of award, produce a bulk pilot lot (to support at least 5000 clinical doses) of prototype MVA vaccine, in a formulation that represents the process to be scaled up for subsequent large-scale production. This lot of vaccine is to be produced under manufacturing conditions necessary to support the use of this product under IND and future large-scale manufacturing. ***(See Note #1 to Offeror.)***

2. Milestone 2: Within six months of award of Part A, provide the NIH with 5000 doses of the final vaccine prototype, filled, finished and released as single dose vials and all information and authorization necessary to enable the government to file an IND for Phase I clinical trials, excluding only that considered to be proprietary, which may be summarized for NIAID and submitted to the FDA in a separate master file. ***(See Note #2 to Offeror.)***

3. Milestone 3: Within six months of award, assess the protection and immunogenicity provided by MVA vaccine prototypes in appropriate animal models according to protocols approved by NIAID. ***(See Note #3 to Offeror.)***

4. Milestone 4: Within 6 months of award, develop and submit for review and approval to NIAID, a clinical development plan for the evaluation of the vaccine, including protocols for the conduct of Phase I clinical trials (Part A), including the core Phase I requirements described in Attachment I, and protocols for the conduct of Part B optional clinical trials. To facilitate comparison of immunological and safety data currently being derived from ongoing studies of vaccinia, the NIAID will oversee the development of standardized Phase I (Part A) and Part B protocols in order to achieve consensus from all collaborating and participating parties.

   For clinical trials conducted by the contractor under their own IND, the plan must provide information about the contract research organization (CRO) proposed to conduct the trials, including information about clinical personnel, laboratory procedures, proposed sites and timelines for their completion. The plan should describe the operational procedures the company will follow to assure adequate oversight of clinical trials, timely and accurate reporting of information to the FDA, structure and responsibilities of a data and safety monitoring board, as well as policies of how data will be processed, shared and published. The plan should specify how NIAID would be kept apprised of progress and communications with the FDA, including processes to assure NIAID may co-monitor or provide for independent audit of the clinical trial.

   The Government, acting through the NIH, will facilitate attaining necessary resources to ensure that immunological assays from samples obtained in Phase I and Part B trials are evaluated using standardized assays that are currently being characterized and validated.

5. Milestone 5: Upon NIAID approval of the Phase I protocol, the contractor shall initiate Phase I trials. Standardized protocols, central laboratories and characterized reagents shall be used for neutralization and ELISA assays in all human trials.

6. Milestone 6: Within 12 months of the award, provide a feasibility plan to manufacture, formulate, fill and finish, test, and deliver to the Government up to 30 million doses of the candidate MVA vaccine suitable for storage in a stockpile for emergency use. The plan should include proposed steps to be taken to monitor the quality (e.g., stability testing plan) and to replenish the stockpile as needed to maintain its ready availability for emergency use under IND, as well as address the product development path for licensure. Accordingly, manufacturing plans should be designed for manufacture of licensed vaccine, not for retention of the vaccine in an IND status.

   The feasibility plan shall include:

   a. Details of the process to scale-up production, including data to support the approach, i.e., documentation of successful scale-up of similar product class or data from intermediate scales of production;

   b. Timeline for production and delivery of up to 30 million doses of product;

   c. Strategy that will be pursued to seek a U.S. license for the product and to provide continued support for maintaining an active Government-held IND; to include obtaining expanded safety and immunogenicity data in all populations and the plan to meet the requirements of the Animal Efficacy Rule;

   d. Estimate of the cost/dose of up to 30 million doses delivered to the Government for use; and

   e. Plan to monitor (stability testing) and replenish the stockpile as needed in consultation with the managers of the Government stockpile. ***(See Note #4 to Offeror.)***

7. Milestone 7: Within 15 months of award, complete an interim clinical trial report that includes data summary, data analysis and interpretation and conclusions for the Phase I trial. These data may be used by the Government and/or the contractor for consultations with the FDA concerning planning for subsequent product development and clinical trials.

8. Milestone 8: Within 30 months of award, complete Phase I clinical trials and provide a report that captures all Phase I clinical trial follow-up and duration of immunity data. The report will include data summary, analysis and interpretation as well as final conclusions and recommendations.

B. Meetings and Conferences - The Contractor shall participate in regular meetings to coordinate and direct the contract efforts as directed by the NIAID Project Officer. Such meetings may include, but are not limited to, meetings of all contractors to discuss clinical protocol design; meetings with individual contractors and other PHS officials to discuss technical, regulatory and ethical aspects of the program, and meetings with NIH technical consultants to discuss down-selection criteria and technical data provided by the contractor. ***(See Note #5 to Offeror.)***

[END OF STATEMENT OF WORK – PART A]

Statement of Work – Part B (Option)

Independently and not as an agent of the government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government as needed to perform the work described below.

A. In accordance with the NIAID approved development plan for vaccine evaluation set forth in Milestone #4 of PART A's Statement of Work and NIAID approved clinical protocols, conduct expanded Phase II clinical studies in healthy populations (i.e., adult and children) and Phase I and II studies in "at risk" (i.e., immunocompromised) populations.

[END OF STATEMENT OF WORK – PART B (OPTION)]

Attachment I

Core Phase I Requirements – Model Protocol Design

Short Title:	
Accrual Objective:	A minimum of 30 subjects
Accrual Period:	Approximately 1 month
Study Design:	A phase I study for preliminary evaluation of the safety and immunogenicity of an MVA vaccine in vaccinia-naïve healthy adults. • Minimum of 30 subjects. • Two doses of MVA vaccine (10^8 $TCID_{50}$ per dose) will be administered by intramuscular injection not to exceed 0.5 mL per dose on days 0 and 28. • A challenge with undiluted Dryvax vaccine against smallpox (Wyeth) will be administered by scarification with a bifurcated needle on day 112 (84 days after the second dose of MVA vaccine). • After the vaccination with Dryvax, the subjects will be observed every two to three days for evaluation. Photographs (digital) of the vaccination site and measurement of erythema, induration and vesicle size, if any, will be taken and recorded using DMID-approved case report forms for determination of whether or not a "take" (formation of a classical Jennerian vesicle or major reaction as defined in the investigator's brochure for Dryvax) has occurred. • Blood specimens will be drawn for immunological studies (see below) at day 0 (just prior to the first injection of MVA) and days 14, 28, 42, 56, 112, 126, 140, 365, and 730 post-vaccination. • Other groups of subjects may be studied to investigate different routes of administration, dosing schedules (timing and/or numbers of doses), vaccine potencies, and time to Dryvax challenge. If additional groups are studied, those subjects will be in addition to the 30 specified above.
Primary Study Objective:	To provide a preliminary assessment of the safety and immunogenicity of two doses of MVA vaccine under study when given four weeks apart and to define the proportion of individuals who respond to a challenge with Dryvax vaccine applied 84 days after the second dose of MVA with a "take" 6 to 8 days after the Dryvax vaccination.
Study Duration:	Subjects will be followed for at least two years following the vaccination.

Notes To Offerors

Development and Testing of a Modified Vaccinia Ankara (MVA) Vaccine
RFP NIH-NIAID-DMID-03-44

NOTE #1 (refers to milestone #1) - Evaluation of the prototype candidate vaccine must be based on a product that represents pilot scale production for the process that the offeror will take to licensure. Substantiation of the process is required. Specifically, the viral seeds, viral amplification, harvest, purification, and formulation should reflect the processes to be used for the proposed scale up of manufacture. Information on production methods, scale, yield, purity etc must be provided. It is anticipated that the maximum vaccination dose will be 10^8 infectious particles.

NOTE #2 (refers to milestone #2) - Information required to conduct clinical trials under a Government-sponsored Investigational New Drug (IND) includes an investigator's brochure (IB), an investigational plan, the Phase I clinical trial protocol, Pharm/Tox data, previous human data and authorization for the FDA to cross-reference either a Drug Master File (MF) or IND containing information relevant to chemistry, manufacturing and control data about the product. Information on the documents required for submitting an IND for a biological product can be found at http://www.fda.gov/cber/ind/ind.htm.

NOTE #3 (refers to milestone 3) - Data that documents preclinical safety, immunogenicity, and protection in appropriate small animal models will be important in meeting this requirement. Data must include serological responses that demonstrate development of neutralizing antibody levels sufficient to protect in appropriate animal model challenges addressing intranasal and aerosol delivery should be performed . Further characterization of cellular immunity, particularly gamma interferon ELISPOT, is encouraged.

NOTE #4 (refers to milestone 6) - As part of the technical proposal, the offeror must provide documentation of the adequacy of facilities available for scale-up and production of vaccine. Funds will not be provided under the terms of this contract to develop the infrastructure required to implement the plan for scale-up and manufacture. Thus, the government requests information be provided about the Contractor's current manufacturing capabilities, the proposed production plan and the estimated manufacturing capacity available to expedite the manufacture of the specified doses of vaccine in the event of a national emergency. Also, it is to be understood that the proposed manufacturing facility must be operated in compliance with cGMP and be capable of producing ultimately licensable products.

NOTE #5 (refers to Item B, Meetings and Conferences) - For cost proposal purposes, one two-day visit every two months to the NIAID in Bethesda, Maryland for two people will be conducted throughout the contract performance period.

NOTE #6 - Because of the urgent need to defend the American public against agents of bioterrorism, and because of the considerable investment by the Government in research and development required to deliver to the American public the vaccines that are the subject of this RFP and subsequent RFPs, the Government expects/demands/requires that the offeror will take all steps necessary to secure access to all intellectual property, know-how and tangible materials that the offeror needs to fulfill its obligation under the contract. Accordingly, the Government may require evidence that the offeror (1) has secured access to such intellectual property, know-how and tangible materials and/or (2) has a plan to secure access to such intellectual property, know-how and tangible materials.

NOTE #7 - The NIH reserves the right to conduct site visits when deemed essential. This may include site visits during the proposal evaluation process and/or visits to the contractor's facilities during contract performance. Such site visits may include other PHS officials or contractors representing NIH.

NOTE #8 - **It is anticipated that this contract will be awarded in phases aligned with the milestones identified in the Statement of Work. Consequently, cost proposals for Part A and Option Part B should provide a breakdown of costs for each milestone as well as a cost estimate for the entire project. In addition, separate cost proposals for both Part A and Option Part B must be submitted.**

NOTE #9 - The Government recognizes that some offerors may have already completed some of the tasks/milestones identified in the Statement of Work. In such instances, offerors' technical proposal should include sufficient information to support this claim and to allow for appropriate technical evaluation.

NOTE #10 - (refers to the evaluation process for the successful contractor for Part B- Option) It is the intention of the NIAID to convene an independent Blue Ribbon Panel composed of *ad hoc* experts and Government personnel, that will advise the Institute on the selection of the contractor who will be performing Part B of this Statement of Work. This Panel will base its evaluation on all items delivered under this contract as specified in the Statement of Work and the Reporting Requirements included under Section A of this RFP, and any other materials the contractor may submit to assist in the evaluation process. Additionally, other information, including but not limited to evidence of compliance with cGMP requirements, or documentation necessary for IND preparation, received from other Government sources (i.e., FDA, CDC, etc.) will also be considered by the Panel in its evaluation. This evaluation is scheduled to take place approximately 12 months after award of the contract, however, the Government reserves the right to convene the Blue Ribbon Panel and review information that substantially accelerates the ability of the Government to exercise Optional Part B of the Statement of Work.